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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/826,119
Filing Date: April 16, 2004
Appellant(s): KUSAMA ET AL.

Gregory Turocy
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed May 09, 2008 appealing from the Office action mailed on 10/02/07.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Saulle, E. "Rapid communication: Nucleotide sequence of Chamois, Alpine Ibex, and Red Deer tRNA Lys and ATPase8 mitochondrial genes." J Animal Science, Vol. 77, (1999), pp. 3398-3399.

Lowe, T. "A computer program for selection of oligonucleotide primers for polymerase chain reactions." Nucleic Acids Research, Vol. 18, no. 7 (1990), pp. 1757-1761.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 24-25, 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saulle et al. (J Animal Sciences, Vol. 77, pp. 3398-3399, 1999) in view of Lowe et al. (Nucleic Acids Research, Vol. 18, No. 7, page 1757-1761, 1990).

Saulle et al. teach a nucleic acid sequence of ATPase8 mitochondrial gene of claims 24 and 35, comprising primer sequences of SEQ ID No. 3-6 as claimed (see page 3398, col.1, paragraph 5, Accession number AF104682, and also see sequence alignment from GenEmbl. database).

With regard to claim 25 Saulle et al. teach that said nucleic acid is of a ruminant deer (alpine ibex) (see page 3398, col. 1, paragraph 5).

However did not teach the combination of primers or primer pairs.

Lowe et al. teach a method for designing primers and evaluating their performance wherein Lowe et al. disclose a computer program for rapid selection of oligonucleotide primers for polymerase chain reaction (see page 1757, col. 1, abstract). Lowe et al. teach that all primers designed for over 10 gene products were experimentally tested and the results showed that all the amplification products specified by the primers are of the predicted size and also hybridize with the appropriate cDNA or internal oligonucleotide probe (see page 1760, col. 2, paragraph 1).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to combine the known nucleic acid sequence as taught by Saulle et al. with a step of generate primers and designing primers as taught by Lowe et al. to amplify and increase the primer specificity and to detect a ruminant-specific DNA because the ATPase8

mitochondrial gene sequence is known (as taught by Saulle et al.) to an ordinary skill in the art at the time the invention was made, and it is obvious to generate primers from the known sequences as taught by Lowe et al. The ordinary artisan would have had a reasonable expectation of success that such primers or primer pairs generated using known sequences as taught by Saulle et al. in view of Lowe et al. to amplify a ruminant-specific DNA for detection because the claimed primers are functional equivalents of the sequences taught by Saulle et al. and Lowe et al. explicitly taught that all primers designed for over 10 gene products were experimentally tested and the results showed that all the amplification products specified by the primers are of the predicted size (see page 1760, col. 2, paragraph 1). The ordinary artisan would have been motivated to generate a number of said primers and primer pairs for detection of ruminant-specific DNA, such primers and primer pairs are considered functionally equivalent to the claimed primers and primer pairs. Further, selection of specific oligonucleotides for specific Tm represents routine optimization with regard to sequence, length and composition of the oligonucleotide, which routine optimization parameters are explicitly recognized in Lowe et al. (This clearly shows that every primer would have a reasonable expectation of success). As noted in *In re Aller*, 105 USPQ 233 at 235, more particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. Routine optimization is not considered inventive and no evidence has been presented that the probe or primer selection performed was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

(10) Response to Argument*s*

Introduction

The instant independent claim 24 is drawn to a pair primers for detection of ruminant-specific DNA comprising a combination of primers set forth in SEQ ID No. 3 and 4 or SEQ ID No. 5 and 6. Claim 25 further defines ruminant of the independent claim 24. Claim 35 is drawn to a kit for detecting an animal-derived component present in a sample comprising at least one primer pair selected from the combinations of primer pairs. For the purpose of examination primer pairs 3 and 4; and 5 and 6 were elected by the Appellants and were considered.

Thus the current claims are drawn to composition or a kit for detection of ruminant-specific DNA comprising a primer combination of SEQ ID No. 3 and 4 or SEQ ID NO. 5 and 6.

issue

Are the claimed primer pairs non-obvious over the cited prior art?

Prima Facie Case

The prima facie case of obviousness for the primer combination is based upon two references, Saulle et al. (J Animal Sciences, Vol. 77, pp. 3398-3399, 1999) in view of Lowe et al. (Nucleic Acids Research, Vol. 18, No. 7, page 1757-1761, 1990). Saulle et al. a method for detecting ruminant-specific DNA in a sample , detecting various species of ruminants, wherein Saulle et al. teach ATPase8 gene sequence which comprises PCR primer sequences as claimed. Lowe et al. teach selection of all possible PCR primers from a known sequence using a computer program.

The Appellants did not dispute that the references do not teach and suggest each of the primer sequences, but argue that the references did not teach or suggest the combination of the

primer pair for PCR amplification. The Appellants further argue that it is improper to rely on the obviousness of primer designing techniques, since the claims are directed to a combination of specific primer pair. The arguments directed to a specific combination of a primer pair should be found unpersuasive.

Motivation

In addressing the motivation issue, it is important to appreciate how routine and ordinary is the selection of a particular combination of primer pair for amplification of a target gene of interest as taught by Lowe et al. The technique to make the primer or primer pairs is obvious at the time the invention was made and hence the product developed based on the known technique, that is, computer progarm to select and design primers or a combimation of a primer pair to amplify a specific DNA sequence would be obvious, once the target gene sequence is known it is obvious to design a proper combination of primers flanking the target site to amplify the target. In the instant situation, the prior art on record teach the ATPase8 gene target whose sequence is known at the time the invention was made, and the prior art on record, Saulle et al. explicitly teach detection of different species of ruminants using different combinations pf primer pairs in a PCR amplification method. Thus at the time the invention was made, the target nucleic acid (ATPase gene) sequence is known and thus it is obvious to one having ordinary skill in the art how to design a primer or a combination of a primer pair using the currently available techniques as described in the prior art (Lowe et al.), since ATPase8 gene target sequence is known in the art and the general techniques to design a combination of a primer pair is obvious from the know sequence.

On page 5 of the appeal brief, Appellants argue that the cited prior art does not teach comparing multiple DNA sequences as a factor in primer design. Appellants also argue that to

design a primer to detect DNA derived from a ruminant, a specific portion of the entire genome sequence, a specific length of sequence and a specific combination of these sequences are required. Appellants also argue that Saulle et al. does not teach or suggest that the ruminant deer sequence can satisfy the above three requirements and assert that in order to design a specific primer pair using the computer program of Lowe et al. one skilled in the art would not have selected all the above three requirements.

Appellants arguments were found unpersuasive. First, Examiner notes that the instant claims as presented would not require comparing multiple DNA sequences as a factor in primer design. Second, Lowe et al. does teach all the three required factors in designing a primer or a primer pair as discussed in the rejection above. Third, Saulle et al. does teach detection of different ruminant-specific DNA sequences (different species of ruminant deer DNA sequences) and the instant claims do not require that the ruminant deer sequence to satisfy the above three factors for designing the primers, instead the ATPase target sequence taught by Saulle et al. does satisfy all the three factors in designing the primers. Fourth, to design a primer pair to detect a specific target sequence one skilled in the art would require a known target sequence. In the present context the specific target sequence comprising ATPase8 gene is known in the art as taught by Saulle et al. and a PCR amplification method using different primer pairs to detect different species of ruminants as taught by Saulle et al. Further, to design a pair of primers one skilled in the art would require selection of a specific target region from the known sequence as taught by Lowe et al., wherein Lowe et al. explicitly taught designing primers to detect a specific target sequence from the known nucleic acid sequence. Thus it would be obvious to one skilled in the art would combine the known target sequence (ATPase gene sequence) as taught by Saulle

et al. for designing a combination of primer pair as taught by Lowe et al. to amplify said target nucleic acid.

On page 5-7 of the appeal brief, Appellants argue that one skilled in the art would not have expected to obtain primers capable of discriminating between homologous sequences without experimentation to determine which primers actually perform as desired in PCR because Saulle et al. does not teach or suggest whether or not the ruminant DNA can be actually detected without detecting DNAs other than the ruminant DNA. Appellants arguments were found unpersuasive because the PCR primers taught by Saulle et al. are based on ATPase gene sequence and not based on a specific ruminant deer sequence as asserted by the Appellants. With regard to undue experimentation Examiner notes that MPEP cites In re O'Farrell, which states regarding "obvious to try" at page 1682, that, In some cases, what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. E.g ., In re Geiger , 815 F.2d at 688, 2 USPQ2d at 1278; Novo Industri A/S v. Travenol Laboratories, Inc ., 677 F.2d 1202, 1208, 215 USPQ 412, 417 (7th Cir. 1982); In re Yates , 663 F.2d 1054, 1057, 211 USPQ 1149, 1151 (CCPA 1981); In re Antonie , 559 F.2d at 621, 195 USPQ at 8-9. In others, what was "obvious to try" was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it. In re Dow Chemical Co ., 837 F.2d, 469, 473, 5 USPQ2d 1529, 1532 (Fed. Cir. 1985); Hybritech, Inc. v. Monoclonal Antibodies, Inc ., 802 F.2d 1367, 1380, 231 USPQ 81, 90-91

(Fed. Cir. 1 986), cert. denied , 107 S.Ct. 1606 (1987); In re Tomlinson ; 363 F.2d 928, 931, 150 USPQ 623, 626 (CCPA 1966). Thus some undue experimentation with trail and error is permissible in determining obviousness.

On page 6-7 of the appeal brief Appellants argue that Saulle et al. does not teach or suggest primers that discriminate between homologous ATPase targets and Lowe et al. software uses single target DNA sequence to generate all possible primers and does not teach primers that can discriminate between homologuos ATPase targets. Appellants' arguments were found unpersuasive. First, the instant claimed primers (SEQ ID NO. 3-6) are drawn to ruminant DNA sequences and they do not require any non-ruminant DNA sequences as asserted by the Appellants and the comparison of homologous sequences to discriminate ruminant vs non-ruminant DNA sequences is not required by the instant claims thus the arguments based on comparison of sequences to discriminate between two homologous DNA sequences were found unpersuasive. Further, the target ATPase 8 gene taught by Saulle et al. is a known sequence and the primer combination generated by using the known sequence would generate finite number of primer pairs not infinite number. Such primer pairs flanking the target region would amplify the target region that comprises a variation or without variation in that target region, which would discriminate between the species as exemplified by Saulle et al., which teach detection of ruminant deer species.

With regard to reasonable expectation of success of designing primers, Examiner notes that the MPEP 2144.08 states "obviousness does not require absolute predictability, only a reasonable expectation of success; i.e. , a reasonable expectation of obtaining similar properties. See , e.g. , In re O'Farrell , 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988)." In this

factual case, there is express suggestion in the prior art to design a primers from a known target sequence and Lowe et al. explicitly taught that all primers designed for over 10 gene products were experimentally tested and the results showed that all the amplification products specified by the primers are of the predicted size (see page 1760, col. 2, paragraph 1). This is sufficient for a reasonable expectation of success.

On page 7-10, Appellants argue that the cited prior art does not teach the multiple DNA sequences that are required to design primers capable of selecting between ruminants and non-ruminants. Appellant further assert that Lowe et al. teach primers designed by the program will work all the time, however, discriminating primer as claimed will not work all the time, instead the discriminating primer will work on certain sequences and will not work on certain other homologous sequences. Appellants further argue that the 10 gene products taught by Lowe et al. are completely different non-homologous sequences and there is no teaching that one primer designed for one gene being tested for other gene target and Lowe et al. does not teach cross-reactivity of the primers. Appellants' arguments were found unpersuasive. First, as discussed above the instant claims on appeal are drawn to primers to detect ruminant-specific DNA sequences and the arguments based on discriminating primers to detect ruminant vs non-ruminant DNA sequences is irrelevant to the present context. Second, to design ruminant-specific DNA sequences one skilled in the art would select a target sequence specific for ruminant-specific DNA such as (ATPase8 gene as taught by Saulle et al), but not the sequences taught by Lowe et al. The prima facie obviousness is based on the use of a computer program designing primers or primer pairs for PCR amplification using known target sequences, but not based on the 10 different sequences taught by Lowe et al. and the arguments based on cross-

reactivity of the primer pairs is irrelevant to the present context. Third, Saulle et al. does teach different combinations of primer pairs to detect different ruminant deer species. Thus Saulle et al. does teach discriminating primers as asserted by Appellants. Thus it is obvious to one skilled in the art to design combinations of primer pairs to specifically amplify different species of ruminant–DNA sequences using the computer program of Lowe et al. and it is not a requirement that Lowe et al. teach designing a discriminating primer to detect various species of ruminant DNA sequences. Fourth, Appellants have not shown any evidence to show that the primers as claimed discriminate between homologous DNA sequences. Applicants have not shown any unexpexted result or a showing supporting the arguments that the combination of the said primer pairs provide better discrimination of different species of ruminant homologous DNA sequences as compared to the prior art.

It is proper to rely on the obviouness of primer selection techniques since the prior art Saulle et al. suggest the target region (ATPase8 gene) for detection of multiple homologous ruminant-specific DNA sequences and Lowe et al. suggest the use of computer program to design primers or a combination of a primer pair for PCR. The selection would have been obvious, since the prior art teaches ATPase gene sequence as a demostrated target sequence and the prior art provides guidance on how to design a proper combination of primers flanking the target site to amplify the target. One having ordinary skill in the art would know how to design a primer or primers using the currently available techniques as described in the prior art (Lowe et al.), since ATPase gene target sequence is known and detection of different species using different primer pairs is known in the art (Saulle et al.), the general techniques to design a combination of primers is obvious from the know sequence. Further, As noted in *In re Aller*, 105

USPQ 233 at 235,More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. Routine optimization is not considered inventive and no evidence has been presented that the selection of primer GC content , length, and annealing temperatures performed was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art. Therefore, an ordinary artisan would have recognized the expected benefits of designing a combination of primers based on the known primer target regions as demonstrated by the prior art, which would result in an improved detection system of the target gene sequences.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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